

### REMARKS

The Official Action of August 10, 2004 has been carefully considered and reconsideration of the application as amended is respectfully requested.

The specification has been amended to remove the bases for the objections at paragraphs 7, 8 and 9 of the Official Action. With respect to the objection at paragraph 7, a revised Sequence Listing has been submitted wherein the amino residues 219 and 220 have been reversed to correspond with the nucleotide sequence in SEQ ID NO: 1. With respect to the objection at paragraph 8 of the Official Action, the description of Fig. 2 has been amended in accordance with the description in the specification as filed at, for example, page 29, penultimate paragraph. The other objections in paragraph 8 are respectfully believed to have been removed by the Response to Notification of Defective Response dated 13 December 2002, wherein reference in the specification to Figures 3-13 were deleted.

Claim 4 has been amended to depend from claim 2 and thereby to remove the basis for the objection at paragraph 10 of the Official Action in accordance with the Examiner's comments. Claims 25 and 26 have been amended to remove the bases for the rejections under 35 USC 112, second paragraph at paragraph 12 of the Official Action. Specifically, the allegedly objectionable term "unique" has been deleted from Claim 25, and Claim 26 has been amended to recite that the claimed sequences are complementary to the sequences of SEQ ID NO: 1.

With respect to the question raised by the Examiner in the first full paragraph

on page 6 of the Official Action, this is respectfully not a proper issue for consideration under 35 USC 112, second paragraph. The Examiner has not questioned the definiteness of the claim language, but appears to be raising a question of alleged lack of enablement under the rubric of a rejection under 35 USC 112, second paragraph. This is respectfully believed to be improper (see MPEP Section 2173.01: “If the scope of the subject matter embraced by the claims is clear, and applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 USC 112, second paragraph.”; see, also, MPEP Section 2174).

With respect to the rejection under 35 USC 112, first paragraph appearing in paragraph 14 of the Official Action, Applicants respectfully request that such rejection be held in abeyance until the application is otherwise in condition for allowance.

Certain claims stand rejected under 35 USC 102(b) as allegedly being anticipated by Ho et al. Certain claims stand rejected under 35 USC 103(a) as allegedly being unpatentable over Ho et al in view of WO 91/14703 or in view of this combination of references further in view of US Patent 5,830,759. Applicants respectfully traverse these rejections.

Applicants respectfully submit that the cited article to Ho et al is not a “printed publication” under the provisions of 35 USC 102(b) such that the rejection is improper. As discussed in MPEP Section 2128, a reference cannot be a “printed publication” unless it is accessible to the public. A reference is proven to be a

"printed publication" "upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it." *In re Wyer*, 655 F.2d 221, 210 USPQ 790 (CCPA 1981) (quoting *I.C.E. Corp. v. Armco Steel Corp.*, 250 F. Supp. 738, 743, 148 USPQ 537, 540 (SDNY 1966)). For reasons next discussed, Applicants respectfully submit that the cited article was not accessible to the public prior to Applicants' invention:

1) The first publication of HBsAG surface antigen mutants was in the Tawan population in the paper by Hsu H.Y. Chang M.H., Liaw S.H. et al entitled "Changes of hepatitis B surface variants in carrier children before and after universal vaccination in Taiwan" in *Hepatology* 1999:: 30: 1312-1317. Hsu H.Y. is from the Public Health Ministry in Taiwan. Prof D. S. Chen, Prof Liaw Y. F. are top researchers in Taiwan. They did not encounter the 145 glycine to arginine, nor linked it to the clustering as the adw stereotype to their variant. Their work is important as they are an accurate and verifiable source backed by their top hepatologist, Professor Ding Shinn Chen who is their Chief Scientist and also the advisor to the Taiwan Government.

2) The first ever reported linkage of the HBV surface antigen mutant glycine 145 to arginine is the inventors' paper in the U.S. publication, the *Journal of Infection* (2000) 41, 260-264 titled "Intrafamilial evidence of Horizontal Transmission of the Hepatitis B Virus Surface Antigen G145R.". This *Journal of Infection* is a renowned publication and has reputable international referees, who investigate the authenticity

and originality of the articles before any publication, is accepted. They found no pre-publication of clustering of this mutant 145 glycine to arginine, before year 2000 and the inventors' paper was accepted.

3) Professor Arie Zuckerman, Director of the World Health Organisation Collaborating Centre for Reference and REsearch on Viral Diseases at the Royal Free and University College Medical School, Rowland Hill Street, London NW3, 2PF, England has reported that the glycine 145 arginine was found in Singapore. See:

<u>Publication:</u>	Evolution and transmission of hepatitis B virus mutants:
Author:	Oon C.J.
Book title:	Hepatitis in the Asian Pacific Region
Editor:	Arie Zuckerman:
Publication:	The Royal College of Physicians of London, England (1997) 1,177-190.

4) Medline search for new publication in year 2000 revealed no article on the 145 glycine to arginine family clustering, nor from Taiwan.

5) At the World Health Organization's Meeting organized by the Asian Pacific Association for the Study of the Liver from February 19-21 2000, world experts on Viral Hepatitis from 60 countries were gathered to review the global situation on Viral Hepatitis. No clustering of hepatitis B glycine 145 arginine from Taiwan was reported nor, for that matter, the cluster in the family from Taiwan. If it did occur it would have been sensational news, and this information would have been released by

the two top world re-known Taiwan investigators: Professor Ding Shinn Chen from the Viral Hepatitis Research Unit, National Twian University, Taipei and Professor Liaw Yuan-Fan from Taiwan's Liver Research Unit, Chong Gung University, Kaoshing. Other world famous Virologists such as: Professor Ian Gust (Australia), Professor Stephen Lorcarni (Australia), Professor Kunio Okuda (Japan), Professor Colin Howard, Professor ShevSarin (India) -- were present at this meeting and did not report this Taiwan clustering, when cluster was mentioned by the inventors in Singapore. The summary of this W.H.O. meeting revealed no cluster reported from Taiwan before the year 2000 (Feb 19) and the W.H.O. report is published in the following journals:

- (a) Journal of the Medical Association, South East Asia May/June 2000.

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Asian Conference Report:

Asian Pacific Association for the Study of the Liver Commemorative  
International Congress on Viral Hepatitis (Author: Oon C.J.)

- (b) Journal of Gastraenterology Aerology and Hepatology Dec. 2002,

Vol 17, Supplement S437 to 512 (ISSN: 0815-9119)

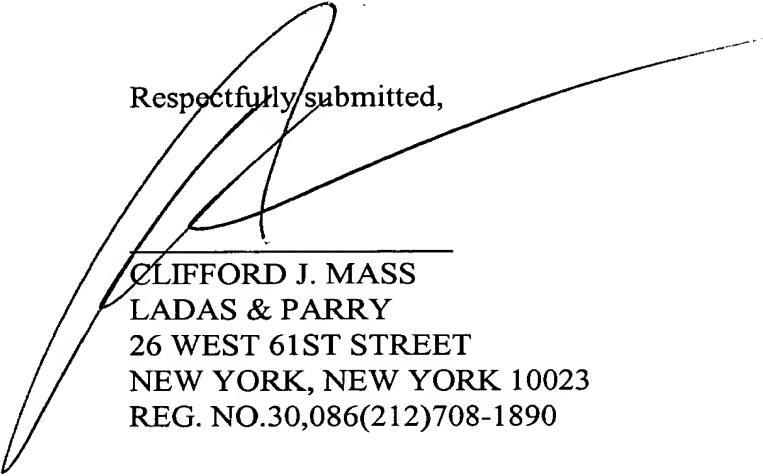
APASL Commemorative International Congress on Viral Hepatitis,  
Prevention and Control.

From the above, it is clear that world experts, including Taiwan's own top hepatitis investigators, did not know of the existence of the Ho et al article or the alleged findings therein as of year 2000. In view of this, and in the absence of any

evidence to show that the subject article was actually disseminated or otherwise made available to the public prior to Applicants' effective filing date, it is respectfully submitted that the prior art rejections should be withdrawn. If on the other hand, the Examiner has evidence to show that the article was accessible to the public, she is respectfully requested to provide the same.

Since all of the objections and rejections of record have been satisfactorily addressed, an early and favorable reconsideration of the application as amended is respectfully requested.

Respectfully submitted,



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